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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,558	07/17/2001	Stefan Dietmar Anker	ICI 102	9145

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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,558	ANKER ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27 and 29-31* is/are pending in the application.

4a) Of the above claim(s) *5-18 and 20-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,19 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/21/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1a. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 April 2006 has been entered.

Status of Claims:

1b. Claims 28 and 32-47 have been cancelled. Thus, claims 1-27, 29-31 are pending, of which claims 1-4, 19, 29-31 are under consideration. Claims 5-18, 20-27 stand withdrawn, however, in the event that the any of the generic linking claims 1, 29-31, become allowable, claims which depend upon and include all the limitations of the allowable claims will be considered for rejoinder. Furthermore, should the rejoined claim be drawn to different inventions, the restriction requirement between the elected invention and the rejoined inventions will be withdrawn.

1c. Receipt of Applicant's declaration under 37 C.F.R §1.132, filed by the inventors of the instant application filed on 14 April 2006 is also acknowledged.

Response to Applicants' Amendment:

2. The following previous objections are withdrawn in light of Applicants amendments filed on 04/14/06:

(i) The rejection of claim 3 made under 35 U.S.C. 112, first paragraph is withdrawn, because claim 3, is drawn to a method of treating cachexia by administering aldosterone antagonists, which is an enabled embodiment.

Specification:

3a. The specification stands objected to under 35 U.S.C. 132(a), because it the deletion of Examples 6 through 9 from the originally filed specification is new matter by omission, since such that the specification is not of the same scope.

Applicants argue that MPEP section 706.03 (o) pertains to an "omission from a step from a method" to broaden the scope, and since this is not the case, in the present application, thus the objection to the specification for deletion is moot.

This is not found persuasive, because omitting examples 6-9 affects the specification as originally filed, and although said omission might not be omitting a step from a method, said deletion results in changing the specification substantially from originally filed.

Drawings:

3b. The drawings stand objected to. Although Applicants have labeled figures 1 and 2 correctly, the amendment fails to label the amended drawing sheets as "Replacement Sheets" as set forth in MPEP § 714 (d). Appropriate correction is required.

Claim rejections-35 USC § 112:

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection of claims 1-3, 19, 29-31 under 35 U.S.C. §112, first paragraph, for not providing enablement commensurate with the scope of the claimed invention is maintained for reason of record. However, the rejection is formulated differently than the previous office actions.

4a. Claims 1-3, 19, 29-31 are rejected under 35 U.S.C. §112, first paragraph, while being enabling for a method of treating the symptoms of cachexia by administering a beta blocker or compounds that inhibit the effect of aldosterone, (i.e an aldosterone antagonists), does not reasonably provide enablement for a method of treating cachexia by administering "all" possible agents which reduce sympathetic nervous system activities.

The instant claims encompass a method of administering unknown agents which reduce "sympathetic nervous system activity", however, the specification teaches that the administration of beta blockers (atenolol and carvedilol) and an aldosterone antagonist (spirononlactone) helped patients gain weight, (see examples 5,7 and 8). The specification showed that the patient treated with carvedilol had improved in exercise capacity and an increase in lean muscle tissue and that the patient tolerated the treatment well. However, Applicants fail to define "SNS activity". The sympathetic nervous system is a system that activates numerous processes. Messages travel through the SNS in a bidirectional flow. Efferent messages can trigger changes in different parts of the body simultaneously, For example, the sympathetic nervous system can accelerate heart rate; widen bronchial passages; decrease motility (movement) of the large intestine; constrict blood vessels; increase peristalsis in the

esophagus; cause pupil dilation, piloerection (goose bumps) and perspiration (sweating); and raise blood pressure. Afferent messages carry sensations such as heat, cold, or pain. The first synapse (in the sympathetic chain) is mediated by nicotinic receptors physiologically activated by acetylcholine, and the target synapse is mediated by adrenergic receptors physiologically activated by either noradrenaline or adrenaline. Therefore, since the specificaiton fails to describe which of these processes the administered agent is supposed to reduce, the skilled artisan would not be able to practice the claimed method. The specification and the claims recite numerous disparate compounds, that do not act through a common mechanism. For example, beta blockers block the action of endogenous catecholamines, epinephrine (adrenaline) and norepinephrine (noradrenaline) in particular, on β-adrenergic receptors, (which is part of SNS system), while aldosterone antagonsits inhibit sodium resorption in the distal tubule of the nephron in the kidneys, and yet again TNF alpha is involved in systemic inflammation. Thus, the recited drugs have different mechanisms of action. Accordingly, the specification is enabling for a method of treating cachexia by administering a beta blocker or compounds that inhibit the effect of aldosterone, (i.e an aldosterone antagonists but is not enabling for he full scope of the claimed invention.

Response to Applicant's arguments:

4b. Applicants argue that the quantity of experimentation necessary to treat cachexia by administering an effective amount of an agent which reduces sympathetic nervous system activity is not undue. Applicants submit that a common mechanism (increased SNS activity) leads to cachexia in a number of patients with different diseases, thus,

cachexia can be treated with drugs that are functionally related by their ability to decrease SNS activity. Accordingly, one of ordinary skill in the art would clearly be able to assess compatibility of the compound to treat cachexia with any medication that the patient might already be taking and that it is not necessary for Applicant to explain drug compatibility.

This argument is found persuasive in part. It is found persuasive in that symptoms of cachectic patients suffering from diverse diseases were treated successfully with beta blockers or aldosterone antagonist. It is also found persuasive in that the skilled artisan would be able to asses drug compatibility with respect to beta blockers or aldosterone antagonist with what ever other medication the patient is taking. However, the argument is not found persuasive regarding decrease in SNS activity being the mechanism of action. The specification discloses and the declaration under 37 C.F.R §1.132, filed by the inventors corroborates that beta blockers (atenolol and carvedilol) and an aldosterone antagonist (spirononlactone) helped patients gain weight, (see examples 5,7 and 8). However, these compounds have different mechanisms of action. Applicants refer to tables A, B and C, however, there are numerous tables in the instant specification, but only one table is labeled as table A. It is unclear which tables are tables B and C. Nevertheless, the specification demonstrates that noradrenaline plasma levels and aldosterone serum levels are elevated in cachetic patients with various diseases. However, as set forth above, the SNS system is a very complex system, and the art does not teach a single SNS activity as implied by Applicants.

Applicants argue that the specification demonstrated common features (SNS activity) shared by cachectic patients arising from a wide range of different underlying conditions. Applicants contend that cachectic patients can be treated with the agents listed on page 4 to page 10. Applicants direct the Examiner's attention to "COMET study" by Dr. Anker.

This is not found persuasive, because the specification only demonstrates that beta blockers and aldosterone antagonists were able to help patients gain weight. Only compounds that have similar mechanism of action as these compounds, are therefore, enabled. The "COMET study" addresses specific compounds, namely Ace inhibitors and beta blockers.

Accordingly, the instant specification is enabling for a method of treating symptoms of cachexia by administering a beta blocker or compounds that inhibit the effect of aldosterone, (i.e an aldosterone antagonists). The term "SNS activity" is not defined in the specification and the art does not recognize a SNS activity, but a very complex system that involves many activities and many processes.

4c. Claims 1-4, 19, stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in the office actions.

Applicants argue that the written description for a claimed genus may be satisfied through a sufficient description of a representative number of species, or by disclosure of structure or other physical and /or chemical properties, by functional characteristics, coupled with a known or disclosed correlation between function and structure. Applicants further argue that they do not have to disclose all possible compounds that

reduce SNS activity. Applicants submit that they have described a common mechanism (increased SNS activity), and described a representative number of species. Thus applicants conclude that claims 1-4 and 19 satisfy the written description.

This has been fully considered but is not deemed persuasive.

The claims do not recite a structure for the agents to be administered, they are only defined by function. Contrary to Applicants argument, the specification only established a correlation between beta blockers and aldosterone antagonist and cachexia. Neither the claims nor the specification describes a representative number of agents that reduce a SNS activity that are used to treat cachexia. Furthermore, since there is no common structure for all of the encompassed agents and there is no one single art recognized class of compounds, the skilled artisan would not recognize that all of the encompassed compounds would be useful in the claimed method. The claims encompass yet to be discovered agents. Therefore, claims 1, 2, 3, 4 and 19 fail to satisfy the written description provision under 35 U.S.C. §112, first paragraph.

Claim rejections-35 USC § 102:

5a. Claims 1-4, 19, 29-31 stand rejected under 35 U.S.C § 102(b) as being anticipated by RALES investigators (October 1996), for reasons of record set forth in the office actions.

Applicants argue that the instant claims recite a method of treating cachexia. Applicants contend that the population treated with spironolactone in the RALES study is not the same population as specified in the amended claims. RALES describes treating patients with chronic heart failure with spironolactone. Applicants argue that

RALES does not disclose or suggest slelcting patients with cachexia not does it disclose that patients treated with spironolactone experienced weight gain. Applicants contend that the claims require selection of the patient on the basis of cachexia. Furthermore, Applicants reiterate that not all patients with heart failure have cachexia. Applicants submit numerous references that teach that not all treatments for heart failure lead to weight gain and that treatment of heart failure would not necessarily treat chachexia. Applicants' arguments and all the submitted references have been considered, but are not deemed persuaisve. RALES study discloses a method of administering spironolactone to patients with severe congestive heart failure who had symptoms of congestive heart failure classes II-IV of New York Heart Association Functional Classification. Thus, it appears that some of the patients treated with spironolactone in the RALES study, might be also be cachectic patients, given their classification. Although the RALES study did not select cachectic patients per se, there is no way to rule out that some of the patients that had NYHA class II-IV were not cachectic.

Therefore the RALES reference anticipates the instant claims 1-4, 19, 29-31.

6. The declaration under 37 C.F.R §1.132, filed by the inventors of the instant application is not sufficient to overcome the rejection of claims 1-4, 19 and 29-31 made under35 U.S.C. §112, first paragraph.

The declaration submits several studies that demonstrate carvedilol (beta blocker), bisoprolol (beta blocker) and spironolactone (aldestrone antagonist) are used to treat cachexia of patients that suffer different diseases. However, as set forth above, these compounds have specific actions. Again the SNS is a very complex system and

involve numerous processes, thus one single activity does not define this system. With respect to the argument that cachetic patients could have different diseases, this is found persuasive. It is acknowledged that patient populations that suffer from different diseases could benefit from beta blocker or aldestrone antagonist.

New Rejections:

Claim Rejections - 35 U.S.C. § 112, second paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-4, 19, 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claim 1 recites "sympathetic nervous activity", however, the specification does not describe which activity is being referred to. Therefore, the claim is indefinite because the metes and bounds of the claim cannot be ascertained, since it is unclear which activity is desired to reduce.

Claims 2-4, 19 and 29-31 are rejected in so far as they depend from claim 1.

Conclusion:

9. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fozia Hamud
Patent Examiner
Art Unit 1647
22 July 2006

Eileen B. O'Hara

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